

Docket No.: 21581-00240-US
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Reissue Patent Application of 6,340,767:
Akira Nishiyama, et al.

Application No.: Not Known

Confirmation No.:

Filed: Concurrently Herewith

Art Unit: N/A

For: **PROCESSES FOR THE PREPARATION OF
5-HYDROXY-3-OXOPENTANOIC ACID
DERIVATIVES**

Examiner: Not Yet Assigned

INFORMATION DISCLOSURE STATEMENT (IDS)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 CFR 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed less than three months after the U.S. filing date, OR less than three months after the date of entry of the national stage of a PCT application, and/or before the mailing date of the first Office Action on the merits.

A copy of each reference on PTO/SB/08 is attached.

A concise explanation of relevance of the items listed on form PTO/SB/08 is given for each listed item.

The following is a brief discussion of the references cited in the IDS.

(1) US 5,155,251

This document suggests that the compound of formula I is prepared by treating a compound of Formula II with a compound of Formula III wherein R₂ is zinc, magnesium, lithium, sodium, or potassium in an aprotic solvent at about -80°C to about 10°C in the presence of additional compound of Formula III or a base such as lithium diisopropylamide, and optionally in the presence of added salt such as zinc chloride, lithium chloride, cerium chloride and the like to afford the compound of formula I (col.4, line 24 to col.5, line 4).

Col.7, lines 13-34, suggests that to a stirred -50°C solution of lithium diisopropylamide is added tertiary-butyl acetate and the mixture is stirred at -45°C to -5°C. (R)-4-cyano-3-hydroxybutyric acid, ethyl ester is then added to the previous mixture. The reaction mixture is stirred for 30 minutes at -5°C to -30°C to afford (5R)-1,1-dimethylethyl 6-cyano-5-hydroxy-3-oxo-hexanoate.

Col.7, lines 36-53, states that to a stirred -50°C solution of tertiary-butyl acetate, (R)-4-cyano-3-hydroxybutyric acid, n-butyl ester and tetrahydrofuran is added lithium diisopropylamide and the mixture is stirred at -45°C to -5°C to afford (5R)-1,1-dimethylethyl 6-cyano-5-hydroxy-3-oxo-hexanoate.

Amended claim 1 recites a step of permitting a lithium amide of formula (III) to act upon a mixture of an acetic acid ester of formula (I) and a 3-hydroxypropionic acid derivative of formula (II) at a temperature not below -20°C, wherein a magnesium halide is added in permitting the lithium amide to act.

US 5,155,251 does not disclose or suggest the claimed addition of a magnesium halide in the step of permitting a lithium amide of formula (III) to act upon a mixture of an acetic acid ester of formula (I) and a 3-hydroxypropionic acid derivative of formula (II) at a temperature not below -20°C.

The present invention according to claim 1 employs the magnesium halide to increase reaction yields dramatically, which were shown in Example 4 (65%) vs. Example 3 (6%), and also in Example 7 (46%) vs. Example 6 (26%) in the instant specification.

Claim 6 recites a Grignard reagent of formula (V), and Claim 10 recites a magnesium-containing compound of formula (VI).

US Patent 5,155,251 does not disclose or suggest these compounds.

(2) US 4,970,313

This patent suggests a step of converting a compound of formula VII, or the corresponding alcoholate thereof, by customary condensation with t-butyl acetate, or a suitable equivalent such as malonic ester, into a compound of formula VIII (col.3, lines 64-68).

Col.5, lines 40 to 53, states that the above condensation is carried out with, for example, t-butyl acetate, preferably with the lithium enolate of t-butyl acetate, in a solvent at -78°C to room temperature, preferably between -30°C and -10°C. The lithium enolate is prepared by the customary methods, preferably using lithium diisopropylamide at -70°C to -50°C. One possible version of the process comprises the use of the compound VII in the form of its alcoholate, specifically as, for example, the lithium, sodium or magnesium alcoholate.

Col.9, lines 1-26, suggests that the mixture resulting from reaction of n-butyllithium with diisopropyl amine was cooled to -70°C and n-butyl acetate was added dropwise. After 1 h at -70°C, the compound from Example 1 (S-3-hydroxy-4-(t-butyldiphenylsilyloxy)butyrate of formula VII) was added dropwise. After 1.5 h at -70°C, the temperature was allowed to rise slowly to -15°C to give (5S)-5-hydroxy-3-oxo-6-(t-butyldiphenylsilyloxy)hexanoate of formula VIII.

Thus this patent merely suggests that the reaction of lithium diisopropylamide with butyl acetate is followed by the addition of the above S-3-hydroxy-4-(t-butyldiphenylsilyloxy)butyrate to the resulting mixture.

Concerning claim 1, this patent does not disclose or suggest the claimed step of permitting a lithium amide of formula (III) to act upon a mixture of an acetic acid ester of formula (I) and a 3-hydroxypropionic acid derivative of formula (II) at a temperature not below -20°C. Further, this patent does not disclose or suggest the claimed addition of a magnesium halide in such a step.

Claim 6 recites a Grignard reagent of formula (V), and a step of permitting a lithium amide of formula (III) to act upon the mixture of a magnesium-containing compound of formula (VI) and an acetic acid ester of formula (I) at a temperature not below -20°C. Claim 10 also recites the above step.

This patent fails to disclose or suggest the Grignard reagent of formula (V), and the above step.

(3) "A Highly Stereoselective Route to the Four Stereoisomers of a Six-Carbon Synthon"
Tetrahedron: Asymmetry, 1 (1990) No.5, pages 307-310, XP 000142279

This publication suggests that compound 5 on treatment with 4.4 equivalents of t-butyl lithioacetate in THF at -78 to 0°C gave the hydroxyketoester 6 (page 308, paragraph 2).

Concerning claim 1, this publication fails to disclose or suggest the claimed step of permitting a lithium amide of formula (III) to act upon a mixture of an acetic acid ester of formula (I) and a 3-hydroxypropionic acid derivative of formula (II) at a temperature not below -20°C; and the claimed addition of a magnesium halide in such a step.

Claim 6 recites a Grignard reagent of formula (V), and Claim 10 recites a magnesium-containing compound of formula (VI).

This publication does not disclose or suggest these compounds.

(4) JP 04 173767 A

This document suggests that a compound of formula I is allowed to react with a compound of formula II, preferably lithium enolate prepared by reacting t-butyl acetate with lithium diisopropylamide at -100 to 20°C, preferably -80 to 0°C to give a compound of formula III (English abstract).

Concerning claim 1, this document fails to disclose or suggest the claimed step of permitting a lithium amide of formula (III) to act upon a mixture of an acetic acid ester of formula (I) and a 3-hydroxypropionic acid derivative of formula (II) at a temperature not below -20°C; and the claimed addition of a magnesium halide in such a step.

Claim 6 results a Grignard reagent of formula (V), and Claim 10 recites a magnesium-containing compound of formula (VI).

This document does not disclose or suggest these compounds.

(5) EP 1,024,139 A, WO 00 08011 A, US 6,472,544 B1 and US 2003-0040634-A1 (These four documents belong to one patent family.)

(5-1) EP 1,024,139 A

EP 1,024,139 A is not a prior art to the instant claims under 35 USC 102(a) and (b) because EP 1,024,139 A was published on August 2, 2000.

It is noted that the instant application was filed on June 2, 2000 as an International Application.

(5-2) WO 00 08011 A

WO 00 08011 A could qualify as prior art under 35 USC 102(a), but not under 102(b) because WO 00 08011 A was published on February 17, 2000, less than one year prior to the filing of PCT/JP/03574.

However, attached hereto are English language translations of the priority documents of the instant application: JP Hei 11-158033 and JP 2000-023804, which were filed before the JPO

on June 4, 1999 and February 1, 2000, respectively. Both the priority documents were filed prior to February 17, 2000 and the latter JP 2000-023804 describes all of the subject matter of the instant claims.

The filing of the English translations is not to be construed as an admission, estoppel or acquiescence. See *Greenwood v. Hattori Seiko Co.Ltd*, 14 USPQ2d 1479 (Fed. Cir.1990).

(5-3) US 6,472,544 B1

US 6,472,544 B1 is not a prior art under any sections of 35 USC 102 because it has a patent date of October 29, 2002 and has a 371 (c)(1), (2), and (4) date of August 16, 2000.

(5-4) US 2003-0040634-A1

US-2003-0040634-A1 is not a prior art under any items of 35 USC 102 because it is a division from the application that matured into the above US 6,472,544 B1, and was published on February 27, 2003.

In accordance with 37 CFR 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR 1.56(a) exists. In accordance with 37 CFR 1.97(h), the filing of this Information Disclosure statement shall not be construed to be an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

It is submitted that the Information Disclosure Statement is in compliance with 37 CFR 1.98 and the Examiner is respectfully requested to consider the listed references.

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The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 22-0185, under Order No. 21581-00240-US. A duplicate copy of this paper is enclosed.

Dated: 11-12-03

Respectfully submitted,

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